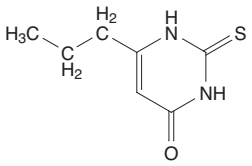
Propylthiouracil

CAS No. 51-52-5

Reasonably anticipated to be a human carcinogen

First listed in the *Fourth Annual Report on Carcinogens* (1985)

Also known as 6-*n*-propylthiouracil or PROP



Carcinogenicity

Propylthiouracil is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Oral exposure to propylthiouracil caused benign or malignant thyroid tumors (follicular-cell adenoma or carcinoma) in four species of rodents: mice (of unspecified sex), rats and hamsters of both sexes, and male guinea pigs. Some metastases were observed in hamsters. Propylthiouracil also caused benign tumors of the anterior pituitary gland (chromophobe adenoma) in mice. It was administered to mice in the diet and to the other rodents in drinking water (IARC 1974, 1982).

Since propylthiouracil was listed in the *Fourth Annual Report on Carcinogens,* an additional study in rats has been published, which reported that propylthiouracil administered in drinking water also caused parathyroid tumors (Walker *et al.* 1994).

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to propylthiouracil. There has been one case report of acute myeloblastic leukemia in a woman following propylthiouracil treatment (Aksoy *et al.* 1974).

Properties

Propylthiouracil is a thioamide compound that exists as a white crystalline powder at room temperature. It is slightly soluble in water, sparingly soluble in acetone and ethyl alcohol, and practically insoluble in ether, chloroform, and benzene. It is stable under normal temperatures and pressures (Akron 2009). It forms complexes with metals and reacts with sulfhydryl-oxidizing agents (IARC 1974, HSDB 2009). Physical and chemical properties of propylthiouracil are listed in the following table.

Property	Information
Molecular weight	170.2[a]
Melting point	219°C to 221°C[a]
Log K_{ow}	0.98[a]
Water solubility	1.2 g/L at 25°C[a]
Vapor pressure	6.92×10^{-8} mm Hg at 25°C[b]
Dissociation constant (pK_a)	7.63[c]

Sources: [a]HSDB 2009, [b]ChemIDplus 2009, [c]Akron 2009.

Use

Propylthiouracil has been used since the 1940s as an antithyroid agent for the treatment of hyperthyroidism (IARC 1974, 2001, Farwell and Braverman 2001). It may also be given to patients with alcoholic liver disease and was shown to decrease mortality by half in these patients in a two-year double-blind study (Orrego *et al.* 1987). Propylthiouracil is also used to test taste perception for bitterness (Ly and Drewnowski 2001); in this context, it is referred to as 6-*n*-propylthiouracil (PROP). The ability to taste PROP is genetically determined and affects an individual's food choices in daily life. Propylthiouracil was formerly used as a metabolic depressant to promote fattening of cattle (IARC 1974, 2001).

Production

In 2009, propylthiouracil was produced by two manufacturers in Europe, two in China, and none in the United States (SRI 2010) and was available from 25 suppliers, including 10 U.S. suppliers. No data on U.S. imports or exports of propylthiouracil were found.

Exposure

The primary route of potential human exposure to propylthiouracil is ingestion as a drug. Three pharmaceutical products approved by the U.S. Food and Drug Administration contain 50 mg of propylthiouracil as the active ingredient (FDA 2009). The initial dose in adults is usually 300 mg per day in three equal doses, and the maintenance dose is 100 to 150 mg per day. In children, the initial dose is 5 to 7 mg/kg of body weight per day administered in three equal doses, and the maintenance dose is one third to two thirds of the initial dose (Drugs.com 2010). Occupational exposure may occur during the production, formulation, packaging, or administration of pharmaceutical products containing propylthiouracil. The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 3,331 workers, including 1,666 women, mostly in the Health Services industry, potentially were exposed to propylthiouracil (NIOSH 1990).

Regulations

Consumer Product Safety Commission (CPSC)

Any orally administered prescription drug for human use requires child-resistant packaging.

Environmental Protection Agency (EPA)

Resource Conservation and Recovery Act

Listed as a hazardous constituent of waste.

Food and Drug Administration (FDA)

Propylthiouracil is a prescription drug subject to specific labeling requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

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